

CLAIMS

1. A divalent antibody fragment comprising two antibody heavy chains
5 and at least one polymer molecule in covalent linkage, each heavy
chain being covalently linked to the other by at least one non-
disulphide interchain bridge linking the sulphur atom of a cysteine
residue in one chain to the sulphur atom of a cysteine residue in the
10 other chain, said cysteine residues being located outside of the
variable region domain of each chain, characterised in that at least
one non-disulphide interchain bridge contains a covalently linked
polymer molecule.
2. An antibody fragment according to Claim 1 in which each heavy
15 chain is covalently linked to the other by a single non-disulphide
bridge, said bridge containing a covalently linked polymer molecule.
3. An antibody fragment according to Claim 1 ~~or Claim 2~~ wherein each
heavy chain is paired with a light chain.
- 20 4. An antibody fragment according to any one of Claims 1 to Claim 3
wherein each heavy chain is a V_H-CH1 chain terminally substituted
by a hinge region domain.
- 25 5. An antibody fragment according to Claim 4 wherein each non-
disulphide bridge present links the sulphur atom of a cysteine residue
located in the hinge region domain of one heavy chain, to the sulphur
atom of a cysteine residue in the hinge region domain of the other
chain.
- 30 6. An antibody fragment according to any one of Claim 1 to Claim 5
wherein the polymer is an optionally substituted straight or branched
chain polyalkylene, polyalkenylene or polyoxyalkylene polymer or a
branched or unbranched polysaccharide.
- 35

where
is
a chain

A

Sub A1

Sub A2

09719045-120700

Sub A 2

7. An antibody fragment according to Claim 6 wherein the polymer is an optionally substituted straight or branched chain poly(ethylene glycol) or a derivative thereof.

5

8. An antibody fragment according to Claim 7 wherein the polymer is methoxy(polyethylene glycol) or a derivative thereof.

9. An antibody fragment according to Claim 8 wherein the polymer has a molecular weight in the range from about 25000Da to about 40000Da.

10

Sub A 3

10. An antibody fragment according to any one of the preceding claims wherein each interchain bridge is the residue of a homo- or heterobifunctional cross-linking reagent.

15

11. An antibody fragment according to Claim 10 wherein each bridge is an optionally substituted C₄₋₂₀alkylene chain optionally interrupted by one or more heteroatoms or heteroatom-containing groups.

Sub A 4

20

12. An antibody fragment according to any one of Claim 1 to Claim 11 which is covalently attached to one or more effector or reporter molecules.

25

13. An antibody fragment according to any one of the preceding claims which is able to selectively bind to a cell surface or soluble antigen.

14. An antibody fragment according to Claim 13 wherein the antigen is human tumour necrosis factor- α or a platelet derived growth factor or a receptor thereof.

30

15. A pharmaceutical composition comprising an antibody fragment according to any of the preceding claims together with one or more pharmaceutically acceptable excipients, diluents or carriers.

a